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ISOLATION, PURIFICATION, EVALUATION AND TOXICITY STUDIES OF NATURAL EDIBLE MUCOADHESIVE POLYMERS FROM VARIOUS PARTS OF PLANTS AND COMPARED WITH SYNTHETIC MUCOADHESIVE POLYMERS

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ABSTRACT: Mucilages of plant origin have been used widely as demulcent because of their unique properties to bind with the mucus membrane. Isolation of water-soluble components from the natural edible sources was carried out by cold/hot aqueous extraction process followed by the organic solvent precipitation. The yield of *Pithecellobium dulce* (PD), *Prosopis juliflora* (PJ), *Acacia arabica* (AA) and *Abelmoschus esculanthus* (AE) was \approx 5.49, 4.91, 3.46, 3.87 % w/w respectively to the initial weight. The isolated mucoadhesive materials obtained from natural sources were proved to be safe and free from toxic or adverse effects. Swollen volumes after 24 hours of hydration was found to be 12.1, 12.4, 13.3, and 18.3 indicating their moderate swellability compared to 27.4 of Carbopol 934 P (CP), 25.7 of sodium alginate(SAA), 1.2 of guar gum(GG) and 6.4 of Hydroxy Propyl Methyl Cellulose (HPMC). The moisture sorption capacities of PD & PJ are very less. The loss on drying of PD, PJ and AA & AE were less than the official limit of 6%. The isolated mucoadhesive material possessed comparable shear and tensile strengths to the commercially available generally regarded as Safe (GRAS) category polymers and higher than the other natural polymers such as sodium alginate and guar gum. The FTIR Spectra's of PD, PJ, AA and AE has not undergone any unacceptable interactions compared with the synthetic mucoadhesive polymers. The DSC thermographs of PD, PJ, AA and AE suggest that there are no significant interactions compared with synthetic mucoadhesive polymers.

Keywords: Mucilages of plant, Mucoadhesive polymers, Natural Mucoadhesive polymers, sodium alginate and guar gum

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INTRODUCTION: *Pithecellobium dulce* (Roxb.) Benth (PD), is a species of flowering plant in the pea family of Mimosaceae that is native to Mexico Central America and northern South America.

It is introduced and extensively naturalized in the Caribbean Florida Gum and Southeast Asia like Philippines. It is considered an invasive species in Hawaii.

It is known by the name "Madras thorn" but it is not native to Madras. The name "Manila tamarind" is misleading since it is neither closely related to tamarind nor native to Manila. It is called "seema chintakaya" in Telugu and Used as food, the seed pods contain a sweet pulp that can be eaten raw or prepared as a smoothie.^{1, 2}

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Prosopis juliflora (Sw.) DC.(PJ), is the Mesquite tree grows to a height of up to 12 metres (39 ft) and has a trunk with a diameter of up to 1.2 metres (3.9 ft). Its leaves are deciduous, bi-pinnate, light green compounded with 12 to 20 leaflets. Flowers shortly after leaf development. The flowers are in 5–10cms. long green-yellow cylindrical spikes, which occur in clusters of 2 to 5 at the ends of branches. Pods are 20 to 30 cms. long and contain between 10 and 30 seeds per pod. A mature plant can produce hundreds of thousands of seeds. Seeds remain viable for up to 10 years. The tree reproduces by way of seeds, not vegetatively. Seeds are spread by cattle and other animals that consume the seed pods and spread the seeds in their droppings. The roots are able to penetrate to a great depth in search of water, upto 53 meters (175 feet) and used as forage, wood and environmental management. The plant possesses an unusual amount of the flavanol (-)-mesquitol in its heartwood.³

Acacia Arabica Willd.(AA), is indigenous to Sind in Pakistan. It occurs wild in India and tropical Africa. It is planted for its bark. The tree yields a gum, known as *Acacia Arabica* gum. The bark of *Acacia Arabica* tree contains tannin and gallic acid. The leaves and fruits of the tree also contain tannin and gallic acid and it has healing power and Curative Properties. The leaves, the bark, the pods and the gum of the tree have medicinal virtues values. The leaves and the bark are useful in arresting secretion or bleeding.

The pods help to remove catarrhal matter and phlegm from the bronchial tubes. The gum allays any irritation of the skin and soothes the inflamed membranes of the pharynx, alimentary canal and genito-urinary organs. The bark, fruit and oleo gum resin are used in various Ayurvedic preparations. *Acacia Arabica* bark finds its primary applications in oral and dental hygiene products, burn injuries and in skin diseases.

Being an astringent, twig of *Acacia Arabica* have been used in India as natural tooth brushes in prevention of bleeding gums. In burn injuries, *Acacia Arabica* powder has been stimulates the healing process of burn injuries and controls the scar formation.⁴

Abelmoschus esculentus (L.) Moench (AE), known in many English-speaking countries as lady's fingers, bhindi or gumbo, is a flowering plant in the family of Malvaceae. It is valued for its edible green seed pods. The geographical origin of *Abelmoschus esculentus* Moench is disputed, with supporters of South Asian, Ethiopian and West African origins. The plant is cultivated in tropical, subtropical and warm temperate regions around the world. The name *Abelmoschus esculentus* Moench is most often used in the United States, with a variant pronunciation, English Caribbeanokra. The word okra is of Nigerian origin and is cognate with okwuru in the Igbo language spoken in Nigeria. Okra is often known as "lady's fingers" outside of Africa.

In various Bantu languages, okra is called kingombo or a variant thereof, and this is the origin of its name in Portuguese (quiabo), Spanish (quimbombó or guigambó), Dutch and French, and also possibly of the name "gumbo" used in parts of the United States and English-speaking Caribbean for either the vegetable or a stew based on it. In India and Pakistan and often in the United Kingdom, it is called by its Hindi/Urdu name, bhindi, bhendi, bendai or bhinda.

In Bangladesh and West Bengal, India, it is called dherosh. In Tamilnadu, India it is called vendai kai. In Andhra Pradesh and Karnataka, India it is called benda kayi. In China it is called qiu kui. In Middle East (Arabic speakers) it is called bamia or bamyeh. Unspecified parts of the plant were reported in 1898 to possess diuretic properties, this is referenced in numerous sources associated with herbal and traditional medicine.^{5,6}

Present days, mucoadhesive agents are thoroughly studied for Buccal drug delivery to improve bioavailability, sustain drug release ,by pass first pass metabolism and produce better patient compliance by reducing frequency of administration.⁷ Mucoadhesive agents isolated, purified seeds from *Pithecellobium dulce* (Roxb) Benth (PD), *Prosopis juliflora* (Sw.) (PJ), Gum of *Acacia arabica* Willd (AA) and Fruit of *Abelmoschus esculentus* (L.) Moench(AE), were

evaluated for various *in vitro* mucoadhesion studies and *in vivo* toxicity studies.

In various studies, natural substances were reported mucoadhesive property due to presence of carbonyl group, thiol group, sugars, proteins, carbohydrates, hydroxyl groups, hydrogen bond, amide groups, cations and anions in their composition⁸. Therefore the use of natural mucoadhesive agents for the purpose of keeping the drug for a prolonged period of time in buccal region should be of great interest. Present research work was mainly focused on isolation, purification and evaluation of natural mucoadhesive agents using different *in vitro* mucoadhesion methods and *in vivo* toxicity studies.

MATERIAL AND METHODS: Plants materials was authenticated and specimens were stored at Department of Botany, Osmania University, Hyderabad-500007, Telangana, India wide voucher numbers 0044,0130,0249,0301, Dated:26-11-2013. Chemicals and Reagents used in the present study were of analytical grade.

Isolation and Purification of Mucoadhesive agents:

The mucoadhesive agents were Isolated and purified by the method adopted by Kulkarni et al.⁹

Isolation and Purification of agent from *Pithecellobium dulce* (Roxb) Benth(PD):

Pithecellobium dulce (Roxb) Benth seeds were collected from the Jannaram Village, Adilabad district of Telangana, India in April month. 100 gm of the seeds were soaked in one litre of distilled water for 12 hrs. The tegmens (an outer covering of the seeds) were removed and the white coverings as well as the white portion of the kernels were separated. They were ground to a fine paste and 500 ml of water was added. Stir vigorously for few minutes and kept for 12 hrs. The slurry was filtered through a muslin cloth. The filtrate was collected and kept undisturbed in refrigerator for 12hrs. Upper clear solution was collected by decantation.

The filtrate was precipitated by the addition of 3 volumes of acetone. Stir continuously for 15 min and the precipitated mucoadhesive material was washed thrice with acetone and dried in a vacuum

drier and powdered. The powder was passed through the sieve no 120 and kept in a desiccator for further studies.

Isolation and Purification of agent from *Prosopis juliflora* (Sw.) (PJ): Dried pods of *Prosopis juliflora*(Sw.) were collected from the Thiryani Village, Adilabad district of Telangana, India in June month. The seeds were segregated from the pods and the white mucilaginous covering was isolated from the cleaned seeds by soaking 100 gm in 200 ml of warm water. The seeds were stirred mechanically for 6 hrs at 300 RPM using a common Laboratory stirrer, so as to detach mucoadhesive material from the kernel and the tegmen.

The mucilaginous portions were picked up manually and the aqueous extract of the same was prepared by continuous stirring for 6hrs. Then it was poured to thrice the volume of acetone. Precipitated material was redispersed in water and precipitated again with acetone to get the purified product. Finally the precipitate was dried in a vacuum drier and powdered. Powder was passed through the sieve no. 120 and kept in a desiccator for further studies.

Isolation and Purification of agent from *Acacia Arabica* Willd (AA):100 gm of the gum obtained from the market was powdered and 500 ml of water was added and stirred well with a Laboratory magnetic stirrer for 6 hrs and set aside for 12 hrs. Then the liquid was filtered through a muslin cloth and allowed to stand. By decantation the clear supernatant liquid was obtained and the sediments were rejected. The volume was reduced to half by heating on a rotary vacuum evaporator.

The concentrated extract was precipitated with 3 volumes of acetone, purified by redispersing in water and precipitating with acetone. The precipitate was dried under vacuum desiccators, powdered and passes through sieve no. 120 and kept in a desiccator for further studies.

Isolation and Purification of agent from *Abelmoschus esculentus* (L.) Moench (AE):

Tender fruits were collected from the market in the month of May and washed well with water. They

were cut into small pieces. To this, triple the volume of water was added and heated at 60 °C for 4 hrs on water bath and set aside for 12 hours. Then the liquid was filtered through muslin cloth and allowed to stand. By decantation the clear supernatant liquid was obtained and the sediments were rejected. The volume was reduced to half by heating on a rotary vacuum evaporator. The concentrated extract was precipitated with 3 volumes of acetone and purified by redispersing in water and precipitating with acetone. The precipitate was dried under vacuum desiccators, powdered and passes through sieve no. 120 and kept in a desiccator for further studies.

Toxicity Studies:

Acute toxicity studies: OECD Guidelines No. 420 Female wistar rats (nulliparous and non-pregnant) of 8 to 10 weeks old weighing 200 – 250gms supplied by National Institute of Nutrition, Hyderabad, India, were individually housed in polypropylene cages lined with husk renewed every 24 h in well-ventilated rooms at 22±3°C and RH between 50 to 60, under artificial lighting 12:12 h light and dark cycle in hygienic condition for at least five days prior to the study. The rats were fed with standard laboratory pellet diet (Hindustan lever) and water *ad libitum*. The studies were performed according to OECD Guidelines 420 and the protocol was approved by the Institutional Animal Ethics Committee (GCOP/IAEC/02, Dated: 1.-01-13).

Sighting study:

Animals were fasted over-night prior to dosing and weighed. The test substance was administered to single animals in a sequential manner following the flow charts in Annex 2 of OECD 420. The starting dose for the sighting study was selected from the fixed dose levels of 300 mg/kg (as there is no evidence from *in vivo* and *in vitro* data). The next dose used for this study was 2000 mg/kg. The Test substances were administered orally in a constant volume of 2mL/100g body weight in the form of suspension. After the substance has been administered, food was withheld for a further 3-4 h. A period of at least 24 hours was allowed between the dosing of each animal. All animals were observed for at least 14 days.

Main study:

A total of five female wistar rats were used for each dose level investigated and the animals were made up of one animal from the sighting study dosed at the selected dose level together with an additional four animals. The time interval between dosing at each level was 3 or 4 days.

Observations:

Animals were observed individually after dosing at least once during the first 30 min, periodically during the first 24 h with special attention given during the first 4 h and daily thereafter, for a total of 14 days. All observations were systematically recorded individually for each animal. Observations include changes in skin, fur, eyes, mucous membranes, respiratory, circulatory, autonomic, central nervous systems, somatomotor activity and behavior pattern.

Attention was directed to observations of tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma. Individual weights of animals were determined shortly before the test substance was administered and at least weekly thereafter. Weight changes were calculated and recorded. At the end of the test surviving animals were weighed and then humanely killed. All animals were subjected to gross necropsy and pathological changes were recorded. Microscopic examination of organs was also done for evidence of gross pathology in animals surviving 24 or more hours after the initial dosing.¹⁰

Acute toxicity studies: OECD Guidelines No. 425 Animals were divided into two groups of 3 animals each. Group I was treated with vehicle (distilled water) and was kept as a control. Group II was treated with 5000mg/kg dose according to their body weight. Blood and tissue were collected on 14th day. Hematological and biochemical parameters were measured in treated group as well as in control group. The organs were quickly blotted and weighed in a digital balance. Gross necropsy of heart, liver and kidney were observed.¹¹

Sub-acute toxicity studies: OECD Guidelines No. 407 the plant extracts at the dose of 250, 500 and 1000 mg/kg body weight were administered orally

to 4 groups of six rats respectively to every 24 h for 28 days and control received vehicle at the same volume. The toxic manifestation such as body weight, mortality, and food and water intake was monitored. After 28 days all surviving animals were fasted overnight and anaesthetized with ether. The heparinised blood samples were collected for determining haematological parameters and the serum from non-heparinised blood was carefully collected for determining clinical blood chemistry. Animals were sacrificed after blood collection and the internal organs were removed and weighed to determine the relative organ weights and observed for gross lesions. The internal organs were preserved in 10% buffered formaldehyde solution for histological examination.¹²

Predetermination studies:

All the Predetermination studies were conducted as described below and the results are represented in **Table 1**.

pH: pH of 1% w/v aqueous solutions of isolated mucoadhesive substances were measured by Toshniwal pH meter.

Determination of swollen volume:

Swellability studies were done by dispersing 1 gm of mucoadhesive substance with a few drops of ethanol in a graduated measuring cylinder and were then made up to 50 ml with water. Swollen volume was noted after 24 hours. Swelling capacity was computed according to the following equation:¹³

$$S = (V_2 - V_1) / V_1 \times 100$$

Where

S = % swelling capacity

V₁ = Tapped volume of the material prior to hydration.

V₂ = Volume of the hydrated or swollen material

Moisture Sorption Capacity:

2g of Mucoadhesive substance was accurately weighed and evenly distributed over the surface of a 70mm-tarred Petri dish. The sample was then placed in Thermo lab Humidity chamber at room temperature and relative humidity of 100%. The weight gained by the exposed samples at the end of a five-day period was recorded and the amount of

water sorbed was calculated from the weight difference.¹⁴

Loss on drying:

The powder sample of mucoadhesive material (5 g) in a Petri dish was dried in an oven at 105°C until a constant weight was obtained. The % moisture content was then determined as the ratio of weight of moisture loss to weight of sample expressed as a percentage.¹⁵

Measurement of mucoadhesive strength of polymer:

Thumb's test: Thumb's test is useful in initial screening test parameters. The test is being carried out by means of the force required or the difficulty to pull out the thumb from other finger, when kept in contact by the mucoadhesive material in specific concentration and volume, with respect to contact time.¹⁶

Shear stress method: Several methods have been reported and in most of the cases, *in vitro* models are based on the measurement of shear or tensile strength. Two smooth, polished plexi glass plates of 2.5×7.5 cm were fixed with the help of an adhesive (Araldite). A nylon thread was sandwiched in between the glasses. Another glass plate of same dimension has been taken and one end was fixed with another nylon thread, which was then passed on a pulley and at the end, and provision was provided to add weight. The sandwiched plate was fixed on a flat table as shown in **Fig. 1**.

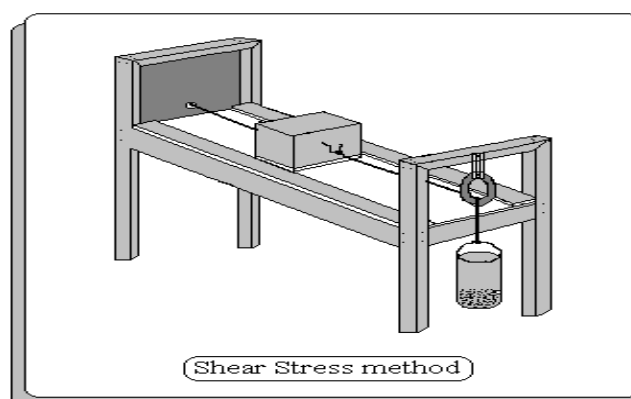


FIG. 1: DESIGN OF MODEL FOR SHEAR STRESS METHOD

Another glass plate fixed with nylon thread was kept in contact between the sandwiched plate by placing appropriate concentrations like 0.5%, 1.0%

and 1.5% w/v of mucoadhesive material in specified volume of 0.5 ml and allowed at specified time intervals of 5,10,15, 20 and 30 minutes. The force required to detach the plates were measured as a means of adhesive strength.¹⁷ This represents the adhesion strength i.e. shear stress required to measure the adhesion and repeated the same procedure for three times.

Park and Robinson Method: This method is based on the measurement of tensile strength. In this method, the force required to separate the bioadhesive sample from freshly excised buccal membrane of goat was determined using a modified instrument as shown in **Fig. 2**. A section of tissue having the mucus side exposed was secured on a glass vial placed in a beaker containing phosphate buffer of pH 6.6. Another section of the same tissue was placed over a rubber stopper, with the mucus side exposed, and secured with a vial cap. Small quantity of polymer solution (1.0%) was placed between two mucosal tissues. The force used to detach the polymer from mucosal tissue was then recorded. The results of the study provided important experimental conditions such as pH, ionic strength, and applied pressure on bioadhesion.¹⁸

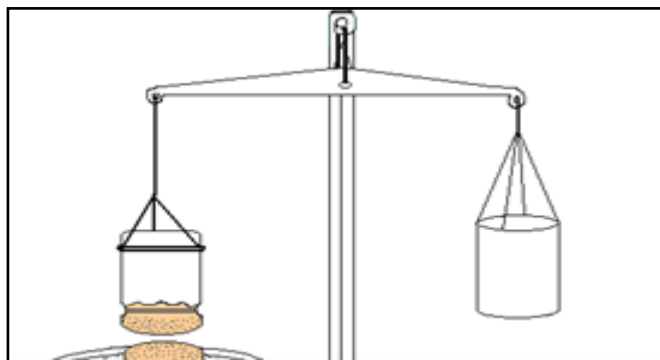


FIG. 2: INSTRUMENTS FOR MEASURING BIOADHESIVENESS BY PARK & ROBINSON METHOD

FTIR studies: The I.R. spectrum of mucoadhesive substances, were recorded individually. The disc was made using 1mg of sample in 100 mg potassium bromide and the spectra were recorded between 4000 cm^{-1} – 400 cm^{-1} using Shimadzu FTIR Spectrophotometer and are shown in Figures 9-12.¹⁹

Differential Scanning Colorimetry: DSC Thermographs of Natural Edible Mucoadhesives

polymers and were recorded between 30.0°C to 300.0°C at the rate of 20.0°C per minute under the environment of nitrogen and the results are provided in **Fig. 13-16**.²⁰

RESULTS AND DISCUSSION: Mucilages or mucopolysaccharides of plant origin have been used widely as demulcent because of their unique properties to bind with the mucus membrane. The selection of the materials for the current investigation was based on their edibility, blandness, availability and the economics.

Isolation of water-soluble components from the natural edible sources was carried out by cold/hot aqueous extraction process followed by the organic solvent precipitation. The selection of the process was based on previous literature giving utmost importance to preserve the components against thermal, enzymatic and hydrolytic degradation. The organic solvents used for precipitation can be recovered back by fractional distillation, making the process more economical. The processes used were found to be effective in selective isolation and purification of the interested constituents and the yielded components possessed good handling properties.

The **Table 1**, represents the details of the extraction processes, respective yields and their physical properties such as pH, swollen volume, swelling capacity, moisture sorption capacity, loss on drying etc.

The yields of PD, PJ, AA and AE were $\approx 5.49, 4.91, 3.46$ & 3.87% w/w respectively to the initial weight. The pH values of 1% w/v solutions of PD and PJ were found to be 5.67 & 6.68 respectively which are very closer to the pH of saliva (≈ 6.6) suggesting its non-irritability to the buccal mucosa. Swelling is the primary characteristic of any material to be a mucoadhesive substance, but over hydration causes slippery surface. Excessive swelling also causes loss of mechanical strength that is required to maintain the structural integrity of the solid dosage forms.²¹ Swollen volumes after 24 hours of hydration were found to be 12.1, 12.4, 13.3 & 18.3 indicating their moderate swellability compared to 27.4 of CP 934 P, 25.7 of sodium alginate, 31.2 of guar gum and 6.4 of HPMC.

Swelling was also assessed by the determination of swelling capacity and moisture sorption profile. Study of moisture sorption is also of considerable importance since it reflects the relative physical stability of dosage forms when stored under humid conditions. In all, this property showed that the AA

powder is sensitive to atmospheric moisture and should therefore be stored in airtight containers. But it was found that the moisture sorption capacities of PJ, AA and PD are very less. The loss on drying of PJ, PD, AA & AE were less than the official limit of 6% stated in British Pharmacopoeia 2004.²²

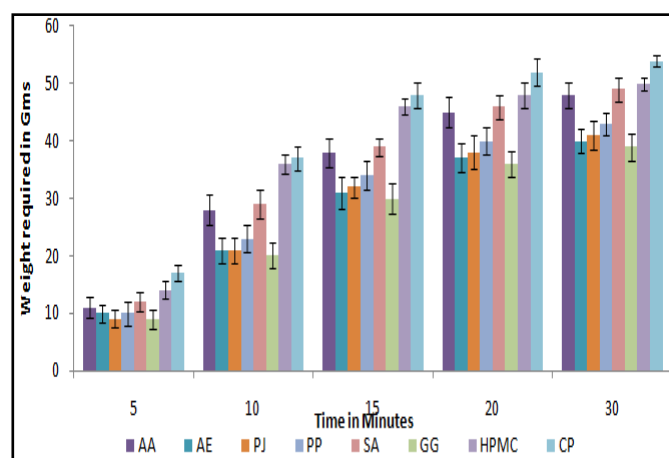
TABLE 1: PHYSICAL PROPERTIES OF MUCOADHESIVE MATERIALS

Mucoadhesive Substance	Biological Source	Part Used	Organic Solvent	Yield %W/W	pH	Swollen Volume (MI)	Swelling Capacity (%)	Moisture Sorption Capacity(%)	Loss On Drying
PD	<i>Pithecellobium dulce</i>	seeds	Acetone	5.49	5.67	12.1 ± 0.4	186.8 ± 5.28	7.6	2.3
PJ	<i>Prosopis juliflora</i>	seeds	Acetone	4.91	6.68	12.4 ± 0.5	156.1 ± 8.17	6.8	1.2
AA	<i>Acacia arabica</i>	gum	Acetone	3.46	3.57	13.3 ± 0.7	167.3 ± 7.18	7.3	4.9
AE	<i>Abelmoschus esculanthus</i>	fruits	Acetone	3.87	4.08	18.3 ± 1.5	387.3 ± 13.78	18.2	5.4
HPMC	**	**	**	**	7.21	6.4 ± 0.7	87.3 ± 3.10	11.2	2.6
CP 934p	**	**	**	**	2.86	27.4 ± 1.1	521.3 ± 10.08	24.1	7.2
SA	**	**	**	**	6.16	25.7 ± 1.6	512.4 ± 11.34	11.3	2.9
GG	**	**	**	**	6.54	31.2 ± 1.5	611.9 ± 18.51	8.7	1.4

The acute and subacute toxicity studies of such extracted sample profile showed that the Natural Mucoadhesive Polymers did not cause any toxic effects on animals. After the observation for 14 days, in the case of sighting study, the data confirmed no hypersensitization of skin and irritation to eyes. No ulceration or inflammation was observed on mucosal membrane and respiratory system respectively. On circulatory system, no sign of cardiac toxicities like increased heart rate, force of contraction or elevated blood pressure was observed. Abnormal toxic effects like neurotoxicity, anxiety or depression was also not observed. The motor coordination and body weight was observed to be normal. Hematological and biochemical parameters showed no changes on the normal blood counts. The heparinised and non-heparinised blood samples also showed normal profile and no gross lesions.

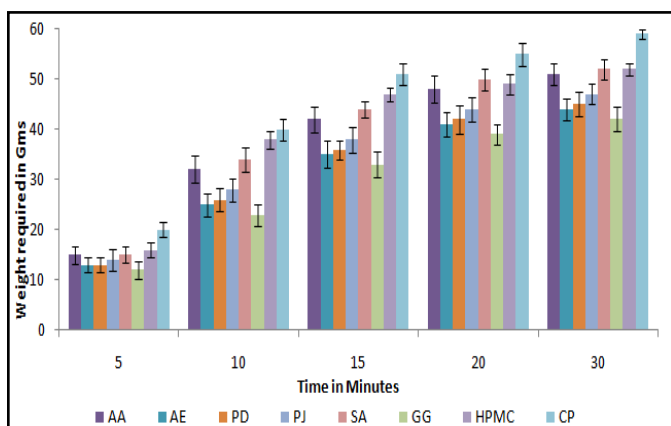
Fig.3-8 represent the weight required to detach the blocks/tissues attached together by the mucoadhesive solutions after specified contact time periods. The results suggest that each isolated mucoadhesive material possessed comparable shear and tensile strengths to the commercially available GRAS (generally regarded as safe) category

polymers and higher than the other natural polymers such as guar gum. Further, these strengths were increased with the increase in concentration but no considerable increase was observed after 15 min of contact time, irrespective of polymers studied. Strengthening of bioadhesion may be due to the formation of more number of secondary bonds as time progresses.



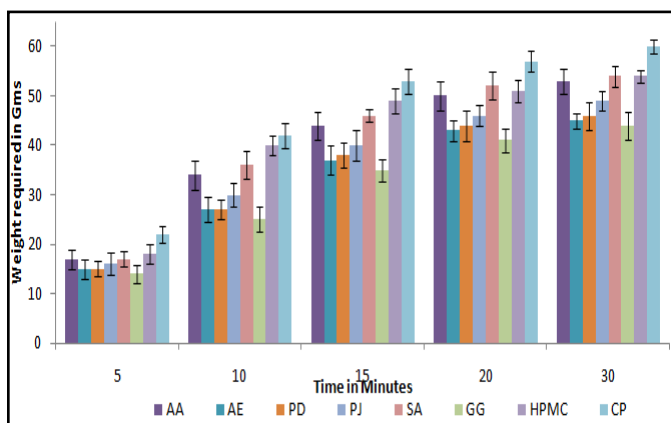
(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG. 3: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (0.5% w/v) BY SHEAR STRESS METHOD



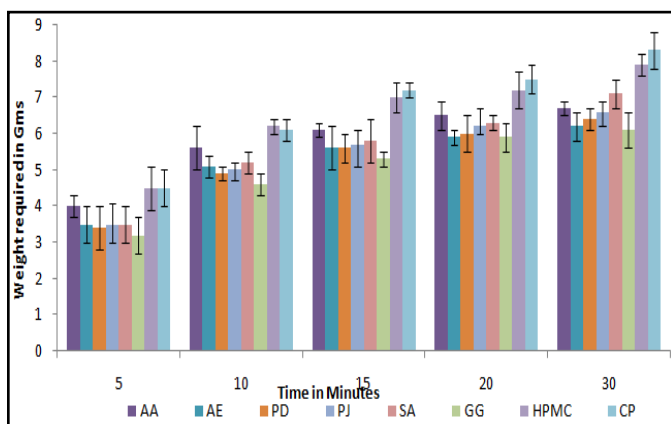
(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG.4: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (1%w/v) BY SHEAR STRESS METHOD



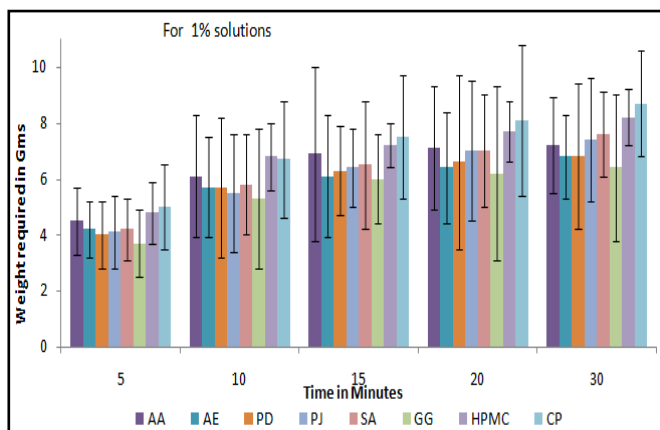
(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal 934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG. 5: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (1.5% w/v) BY SHEAR STRESS METHOD



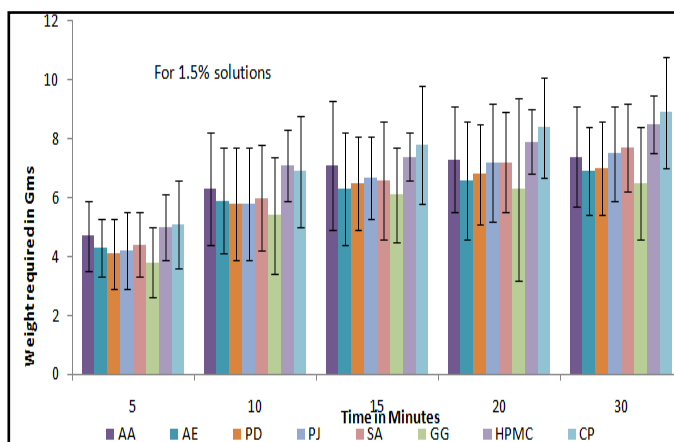
(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG. 6: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (0.5% w/v) BY PARK & ROBINSON METHOD



(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG. 8: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (1%W/V) BY PARK & ROBINSON METHOD



(PD=*Pithecellobium dulce*, PJ=*Prosopis juliflora*, AA=*Acacia Arabica*, AE=*Abelmoschus esculanthus*, CP=Carbopal934, SA=Sodium alginate, GG=Guar gum and HPME=Hydroxy propyl methyl cellulose.)

FIG.8: MUCOADHESIVE STRENGTH OF POLYMER SOLUTIONS (1.5%W/V) BY PARK&ROBINSON METHOD

Fig. 9-12 represent the FTIR Spectra's of mucoadhesive polymers under investigation. Results suggest that Natural Mucoadhesive polymers isolated from the natural edible sources has not undergone any unacceptable interactions compared with the synthetic mucoadhesive polymers.

Fig. 13-16 represent the DSC thermographs of Natural Mucoadhesive Polymers under investigation. The thermographs suggest that there are no significant interactions between the mucoadhesive polymers under investigation with compared with Ynthetic Mucoadhesive Polymers.

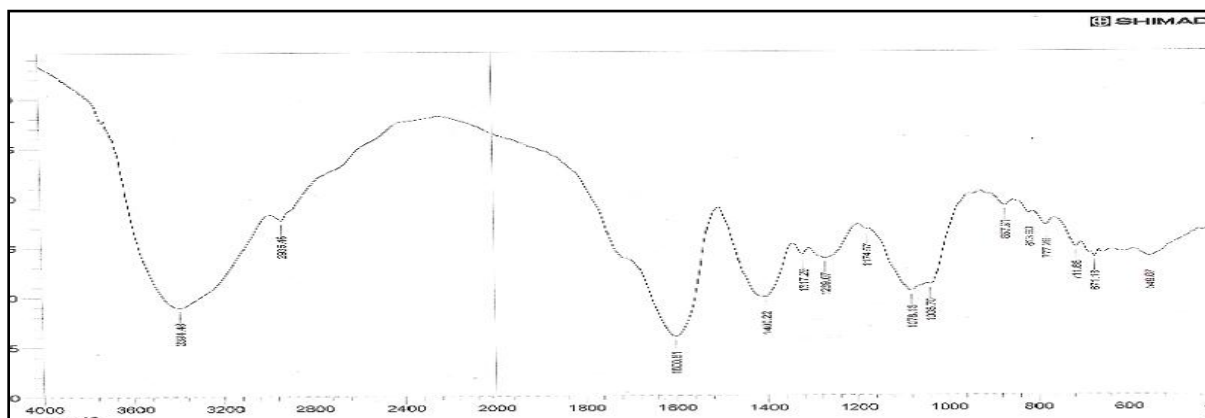


FIG. 9: FTIR SPECTRUM OF *PITHECELLOBIUM DULCE* (PD)

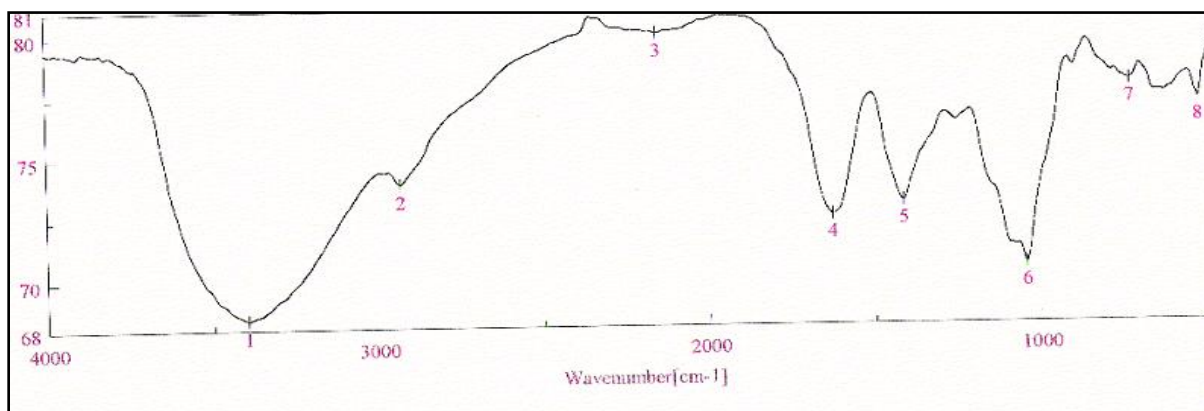


FIG. 10: FTIR SPECTRUM OF *PROSOPIS JULIFLORA* (PJ)

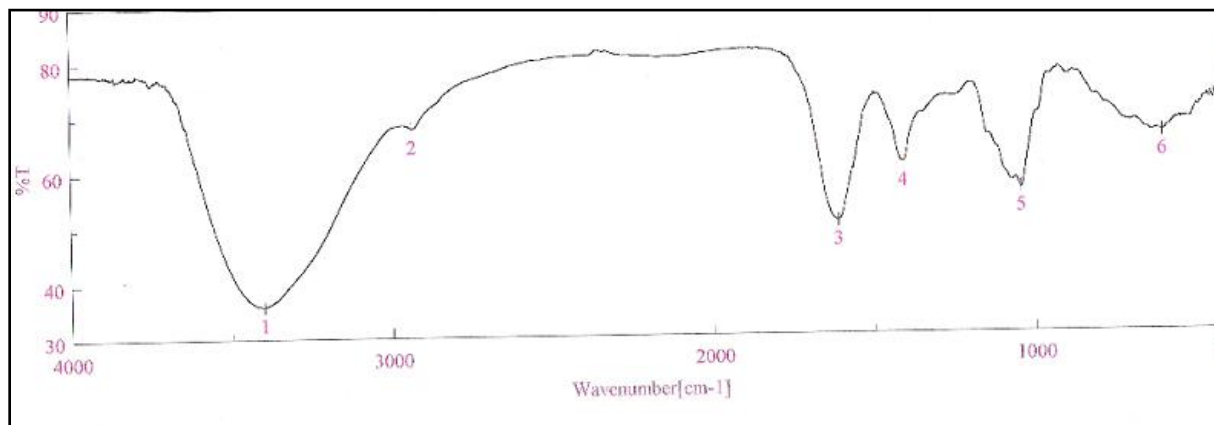


FIG.11: FTIR SPECTRUM OF *ACACIA ARABICA* (AA)

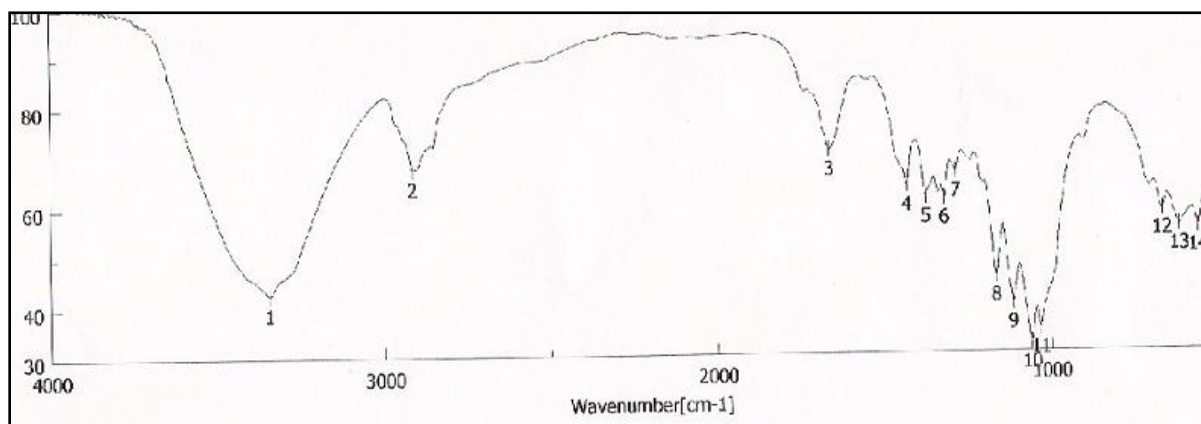


FIG.12: FTIR SPECTRUM OF *ABELMOSCHUS ESCULANTHUS* (AE)

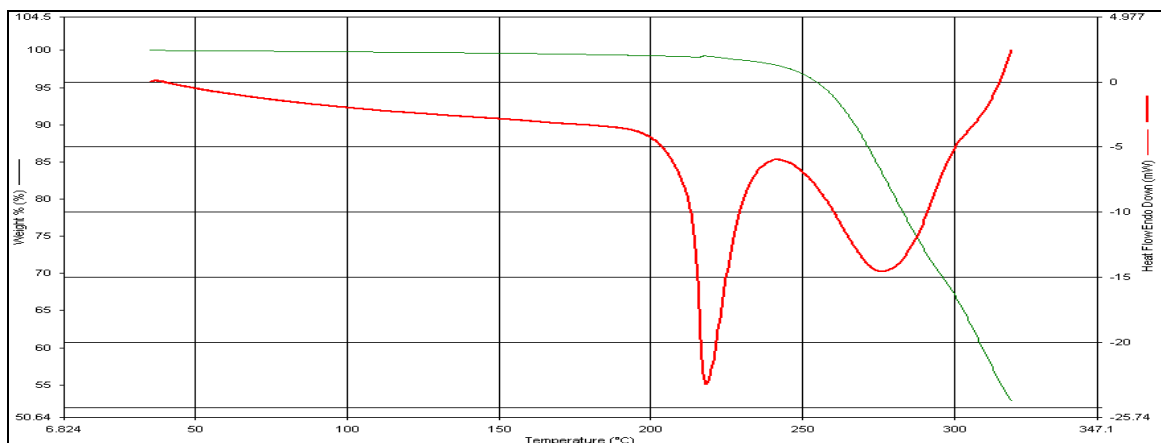


FIG. 13: DSC THERMOGRAPH OF PITHECELLOBIUM DULCE (PD)

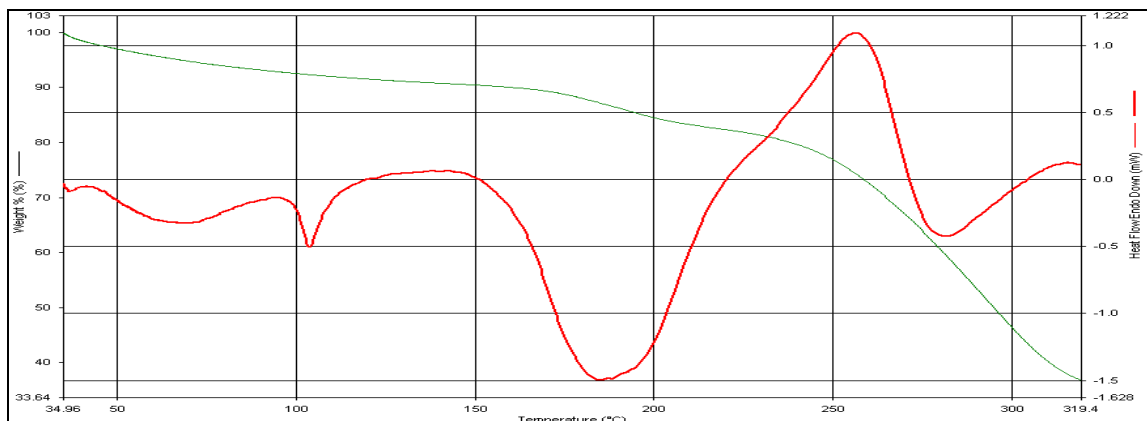


FIG. 14: DSC THERMOGRAPH OF PROSOPIS JULIFLORA (PJ)

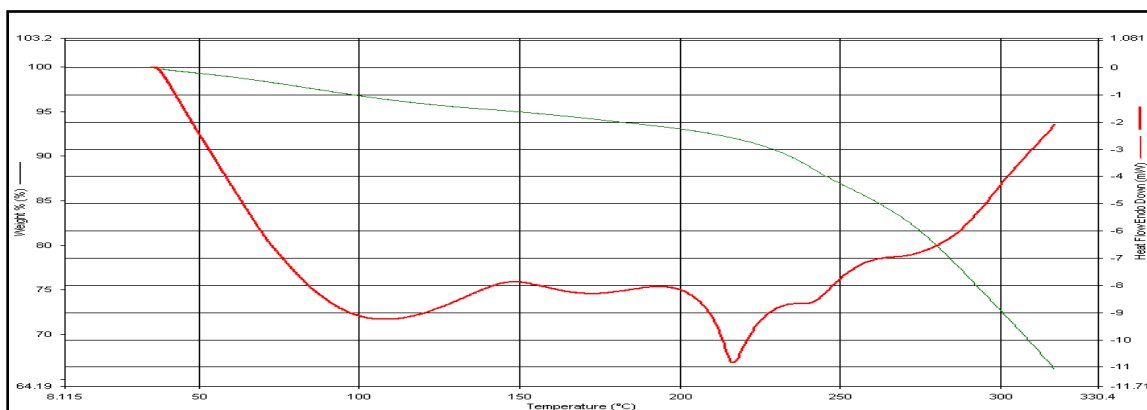


FIG.15: DSC THERMOGRAPH OF ACACIA ARABICA (AA)

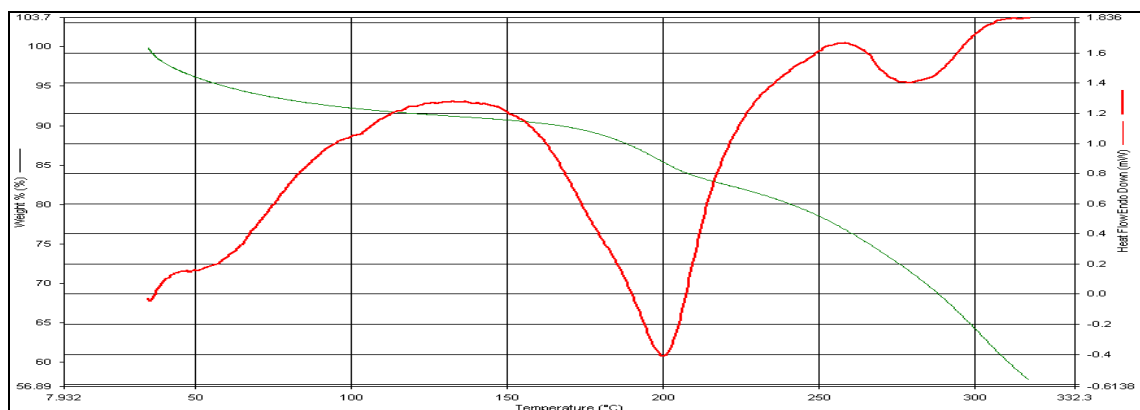


FIG.16: DSC THERMOGRAPH OF ABELMOSCHUS ESCULANTHUS (AE)

SUMMARY AND CONCLUSIONS:

Natural mucoadhesive agents were isolated from the natural edible sources by cold/hot aqueous extraction followed by organic solvent precipitation. The methods used were found to give satisfactory yields and are reproducible. The physical properties of the substances such as pH, swelling, moisture sorption capacity, loss on drying etc were evaluated.

The mucoadhesiveness of aqueous solutions of natural polymers were evaluated by shear stress, Park and Robinson methods and compared with the commercially used GRAS (Generally Regarded as Safe) category polymers HPMC, CP, sodium alginate and guar gum. From these findings, it was evident that the natural mucoadhesive agents possess good handling properties and comparable bioadhesive strengths.

The acute and subacute toxicity studies of extracted samples showed that the mucopolysaccharides did not cause any toxic effects on animals. Hematological and biochemical parameters showed no changes on the normal blood counts.

In the light of the above results it can be concluded that

1. All the materials isolated from natural sources were found to possess good physical characteristics that are essential for utilization as a Mucoadhesive agent for Buccal drug delivery.
2. The pH values of the mucoadhesive substances were nearer to buccal pH, suggesting non-irritability to mucosa.
3. The isolated mucoadhesive materials obtained from natural sources were proved to be safe and free from toxic or adverse effects.
4. The FTIR and DSC studies indicated no remarkable interaction between the Synthetic Mucoadhesive polymers and the Mucoadhesive substances isolated from natural edible sources.

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